

## CLAIM AMENDMENTS

This listing of claims will replace all prior versions, and listings, of claims in the application:

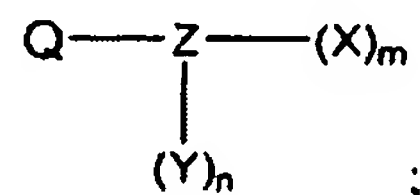
### Listing of Claims:

Claim 1 (previously presented). A method for identifying non-targets of a drug, comprising:

(a) selecting a small organic molecule drug whose non-target proteins with which it interacts are to be identified, and providing a capture compound that presents the drug or a fragment, intermediate, metabolite or prodrug of the drug whose non-target proteins are to be identified, wherein:

the drug, the fragment, intermediate, metabolite or prodrug of the drug interacts with a non-target protein of the drug;

the capture compound has the formula:



X is a photoactivatable group that, upon exposure to light, covalently binds to an amino acid side chain of a protein to effect covalent binding of the capture compound to a protein;

Y is the small molecule organic drug or a fragment, intermediate, metabolite or prodrug thereof for assessing interactions with non-targets;

Q is a sorting function for immobilizing or separating the capture compounds and

Z is a trifunctional amino acid ~~containing 50 or fewer atoms~~ that  
presents each of X, Y and Q;

m is 1; and

n is 1;

(b) contacting the capture compound with a sample containing non-target proteins that interact with Y, wherein contacting is effected under conditions in which X is not activated and for a sufficient time for interaction between the capture compounds and proteins in the sample to reach equilibrium, whereby Y interacts with drug non-target proteins in the sample;

(c) exposing the capture compound to electromagnetic radiation that activates X, whereby X forms a covalent linkage with protein(s) in the sample that are interacting with Y to effect capture thereof; and

(d) determining the identity of captured proteins, wherein the captured identified proteins comprise non-targets of the drug.

Claim 2 (previously presented). The method of claim 1, wherein Z comprises an amino acid; and Q a group for immobilizing or separating the capture compound biotin, (His)<sub>6</sub>, 4,4difluoro-4-bora-3a,4a-diaza-s-indacene (BODIPY), an oligonucleotide, a nucleoside, a nucleotide, an antibody, an immunotoxin conjugate, an adhesive peptide, a lectin, a liposome, a peptide nucleic acid or an activated dextran.

Claims 3 - 4 (cancelled).

Claim 5 (previously presented). The method of claim 1, wherein steps (a)-(d) are performed a plurality of times, each with the moiety Y linked to the moiety Z in a different orientation via a different point of attachment on the Y moiety.

Claim 6 (previously presented). The method of claim 1, wherein:

X is selected from among an azide or a diazine;

Z is an amino acid; and

Q comprises biotin or an oligonucleotide.

Claims 7 - 9 (cancelled).

Claim 10 (previously presented). The method of claim 1, wherein following step (a) or (c), the capture compounds are immobilized on a solid support via Q, which binds to the surface of the support or a molecule thereon.

Claims 11 - 14 (cancelled).

Claim 15 (withdrawn). The method of claim 1, wherein:

Z is a moiety that is cleavable prior to or during mass spectrometric analysis of biomolecules bound to the capture compound.

Claim 16 (cancelled).

Claim 17 (previously presented). The method of claim 1, wherein

Z is a moiety that is not cleavable prior to or during mass spectrometric analysis of biomolecules bound to the capture compound.

Claim 18 (withdrawn). The method of claim 1, wherein:

Q is an oligonucleotide or oligonucleotide analog that includes a single-stranded portion of sufficient length "j" to form a stable hybrid with a base-complementary single stranded nucleic acid molecule or analog.

Claims 19 - 21 (cancelled).

Claim 22 (withdrawn). The method of claim 1, wherein Q has the formula

$N^1_s B_i N^2_u$ , wherein:  $N^1$ , B and  $N^2$  are oligonucleotides or oligonucleotide analogs comprising s, t and u members, respectively;

B is a region of sequence permutations that contains at least two bases; and sum of s, i and u is at least 5.

Claims 23 - 24 (cancelled).

Claim 25 (withdrawn). The method of claim 1, wherein Z is a photocleavable, acid cleavable, alkaline cleavable, oxidatively cleavable, or reductively cleavable group.

Claims 26 - 33 (cancelled).

Claim 34 (cancelled).

Claims 35 - 37 (cancelled).

Claim 38 (cancelled).

Claims 39 - 42 (cancelled).

Claim 43 (cancelled).

Claim 44 (previously presented). The method of claim 1, wherein an X is a diazirine, 3trifluoromethyldiazirine or an azide; Z is an amino acid and Q is biotin.

Claims 45 - 46 (cancelled).

Claim 47 (withdrawn). The method of claim 1, wherein the capture compounds comprise a mass modifying tag linked to Z.

Claims 48 - 54 (cancelled).

Claim 55 (withdrawn). The method of claim 18, wherein capture compounds are hybridized to a plurality of oligonucleotides or analogs thereof that comprise oligonucleotides that are complementary to each Q.

Claim 56 (withdrawn). The method of claim 55, wherein the oligonucleotides or analog thereof that are complementary to Q are immobilized on a solid support as an array.

Claims 57 - 62 (cancelled).

Claim 63 (withdrawn). The method of claim 1, wherein the Z moiety of the capture compound comprises a functionality conferring luminescence, fluorescence, chemiluminescence or colorimetric properties.

Claims 64 - 65 (cancelled).

Claim 66 (withdrawn). The method of claim 1, wherein the capture compounds further comprise a solubility group W that influences the solubility properties of the capture compound.

Claim 67 (withdrawn). The method of claim 1, wherein the selectivity function Y is a drug or drug intermediate/fragment selected from among those set forth in Figure 17 and Figure 21.

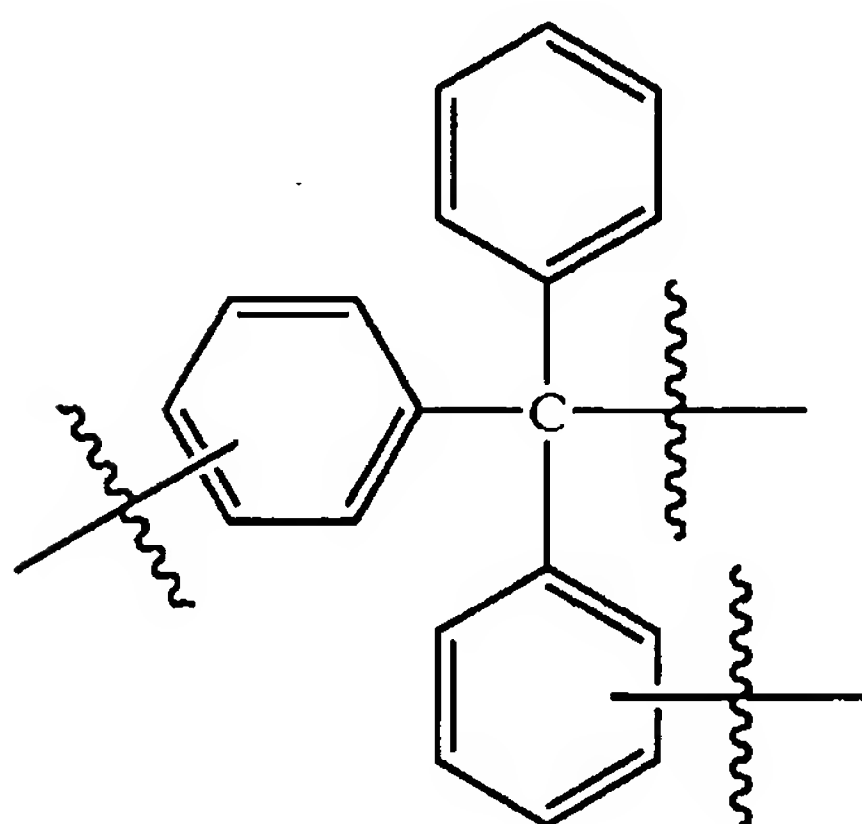
Claim 68 (withdrawn). The method of claim 1, wherein the reactivity function X is selected from those set forth in Figure 16.

Claims 69 - 74 (cancelled).

Claim 75 (previously presented). The method of claim 1, wherein Q is biotin.

Claim 76 (cancelled).

Claim 77 (withdrawn). The method of claim 1, wherein Z has the formula:



Claims 78 - 109 (cancelled).

Claim 110 (previously presented). The method of claim 1, further comprising identifying or detecting a captured biomolecule by mass spectrometric analysis.

Claims 111 - 115 (cancelled).

Claim 116 (previously presented). The method of claim 1, wherein the sample comprises a biological sample, a body tissue or fluid or a cell lysate.

Claim 117 (cancelled).

Claims 118 - 136 (cancelled).

Claim 137 (previously presented). The method of claim 1, wherein:

Q is selected from among biotin, (His)<sub>6</sub>, 4,4-difluoro-4-bora-3a,4a-diaza-s-indacene (BODIPY), an oligonucleotide, a nucleoside, a nucleotide, an antibody, an immunotoxin conjugate, an adhesive peptide, a lectin, a liposome, a peptide nucleic acid and an activated dextran; and

Z has the formula:

$(S^1)_t M (R^{15})_a (S^2)_b L$ , wherein:

S<sup>1</sup> and S<sup>2</sup> are spacer moieties;

t and b are each independently 0 or 1;

a is an integer from 0 to 4;

M is a central moiety possessing three or more points of attachment;

R<sup>15</sup> is a monovalent group independently selected from y ;

y<sup>2</sup> is a divalent group independently having any combination of the following groups: a direct link, arylene, heteroarylene, cycloalkylene,  $>C(R^{17})_h$ ,

C(R<sup>17</sup>)=C(R<sup>17</sup>),

$>C=C(R^{23})(R^{24})$ ,  $>C(R^{23})(R^{24})$ , C=C, O,  $>S(A)u$ ,  $>P(D)v(R^{17})$ ,  $>P(D)v(ER^{17})$ ,

$>N(R^{17})$ ,



$>N(COR^{17})$ ,  $>N+(R^{23})(R^{24})$ ,  $>Si(R^{17})_h$  and  $>C(E)$ ; wherein:

u is 0, 1 or 2;

v is 0, 1, 2 or 3;

A is 0 or  $NR^{17}$ ;

D is S or 0; and

E is S, 0 or  $NR^{17}$ ;

$R^{17}$  and  $R^{18}$  are each independently selected from the group consisting of hydrogen, halo, pseudohalo, cyano, azido, nitro,  $SiR^{27}R^{28}R^{25}$ , alkyl, alkenyl, alkynyl, haloalkyl, haloalkoxy, aryl, aralkyl, aralkenyl, aralkynyl, heteroaryl, heteroaralkyl, heteroaralkenyl, heteroaralkynyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl, heterocyclylalkynyl, hydroxy, alkoxy, aryloxy, aralkoxy, heteroaralkoxy and  $NR^{19}R^{20}$ ;

$R^{19}$  and  $R^{20}$  are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl and heterocyclyl;  $R^{23}$  and  $R^{24}$  are selected from (i) or (ii) as follows:

(i)  $R^{23}$  and  $R^{24}$  are independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl and heteroaryl; or

(ii)  $R^{23}$  and  $R^{24}$  together form alkylene, alkenylene or cycloalkylene;

$R^{25}$ ,  $R^{27}$  and  $R^{28}$  are each independently a monovalent group selected from hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, haloalkoxy, aryl, aralkyl, aralkenyl,

aralkynyl, heteroaryl, heteroaralkyl, heteroaralkenyl, heteroaralkynyl, heterocyclyl,  
heterocyclylalkyl, heterocyclylalkenyl, heterocyclylalkynyl, hydroxy, alkoxy, aryloxy,  
aralkoxy, heteroaralkoxy and  $\text{NR}^{19}\text{R}^{20}$ ;

$\text{R}^{15}$ ,  $\text{R}^{17}$ ,  $\text{R}^{18}$ ,  $\text{R}^{19}$ ,  $\text{R}^{20}$ ,  $\text{R}^{23}$ ,  $\text{R}^{24}$ ,  $\text{R}^{25}$ ,  $\text{R}^{27}$  and  $\text{R}^{28}$  can be substituted with one  
or

Substituent s each independently selected from Z2; Z2 is selected from alkyl,  
alkenyl, alkynyl, aryl, cycloalkyl, cycloalkenyl, hydroxy,  $\text{S}(0)\text{hR}^{35}$ ; h is 0, 1 or 2,  
 $\text{NR}^{35}\text{R}^{36}$ ,  $\text{COOR}^{35}$ ,  $\text{COR}^{35}$ ,  $\text{CONR}^{35}\text{R}^{36}$ ,  $\text{OC}(0)\text{NR}^{35}\text{R}^{36}$ ,  $\text{N}(\text{R}^{35})\text{C}(0)\text{R}^{36}$ , alkoxy,  
aryloxy, heteroaryl, heterocyclyl, heteroaryloxy, heterocycliloxy, aralkyl, aralkenyl,  
aralkynyl, heteroaralkyl, heteroaralkenyl, heteroaralkynyl, aralkoxy, heteroaralkoxy,  
alkoxycarbonyl, carbamoyl, thiocarbamoyl, alkoxycarbonyl, carboxyaryl, halo,  
pseudohalo, haloalkyl and carboxamido; and

$\text{R}^{35}$  and  $\text{R}^{36}$  are each independently selected from among hydrogen, halo,  
pseudohalo, cyano, azido, nitro, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, triarylsilyl,  
alkyl, alkenyl, alkynyl, haloalkyl, haloalkoxy, aryl, aralkyl, aralkenyl, aralkynyl,  
heteroaryl, heteroaralkyl, heteroaralkenyl, heteroaralkynyl, heterocyclyl,  
heterocyclylalkyl, heterocyclylalkenyl, heterocyclylalkynyl, hydroxy, alkoxy, aryloxy,  
aralkoxy, heteroaralkoxy, amino, amido, alkyl amino, dialkylamino, alkylaryl amino,  
diaryl amino and aryl amino.

Claim 138 (cancelled).

Claim 139 (previously presented). The method of claim 1, wherein M is an

amino acid.

Claim 140 (withdrawn). The method of claim 139, wherein X is an azide, S1 and S2 each is independently (CH<sub>2</sub>)<sub>r</sub>, where r is 1-10, and Q is biotin or an oligonucleotide.

Claims 141 - 142 (cancelled).

Claim 143 (withdrawn). The method of claim 1, further comprising re-designing the moiety Y to eliminate or alter its binding interactions with a captured biomolecule.

Claim 144 (previously presented). The method of claim 1, further comprising identifying a function of a captured protein.

Claim 145 (withdrawn). The method of claim 143, wherein the alteration in binding is an increase in binding.

Claim 146 (withdrawn). The method of claim 143, wherein the alteration in binding is a decrease in binding.

Claim 147 (withdrawn). The method of claim 143, wherein the biomolecule for which binding is altered is a non-target biomolecule.

Claims 148 - 150 (cancelled).

Claim 151 (previously presented). The method of claim 1, wherein the sample is contacted with a collection of capture compounds.

Claim 152 (previously presented). The method of claim 1, wherein the X moiety of the capture compound comprises an azide, diazirine or a group which, following activation, reacts with the captured target and non-target proteins.

Claim 153 (withdrawn). The method of claim 143, wherein the method is repeated with the re-designed moiety Y linked to a capture compound to effect further modification thereof.

Claim 154 (cancelled).

Claim 155 (withdrawn). The method of claim 143, wherein the captured biomolecule for which binding is altered is a drug target protein.

Claim 156 (withdrawn). The method of claim 143, wherein the captured biomolecule for which binding is altered is a non-drug target protein.

Claims 157 - 159 (cancelled).

Claim 160 (previously presented). The method of claim 1, wherein a concentration of capture compound is varied in a plurality of different reactions.

Claim 161 (previously presented). The method of claim 160, wherein a dissociation constant ( $K_d$  value) is determined.

Claim 162 (cancelled).

Claim 163 (previously presented). The method of claim 110, wherein mass spectrometric analysis is performed using a mass spectrometric analysis format that is selected from among matrix assisted laser desorption ionization (MALDI), continuous or pulsed electro spray (ES) ionization, ion spray, thermo spray, and massive cluster impact mass spectrometry.

Claim 164 (previously presented). The method of claim 163, wherein the mass spectrometric analysis format is linear time-of-flight (TOF), reflectron time-of-flight, single quadrupole, multiple quadrupole, single magnetic sector, multiple magnetic sector, Fourier transform, ion cyclotron resonance (ICR), or ion trap.

Claim 165 (cancelled).

Claim 166 (previously presented). The method of claim 144, wherein the function of the biomolecule is determined by sequence alignment, pharmacophores, homology models and protein motif correlation, liver microsomes metabolic pathways, cDNA-expressed enzymes, signal pathways and back-mapping to yeast pathways, simulations and protein/protein interaction of pull-out proteins, native polymorphisms, knock-out/knock-in, flow

cytometry, therapeutic activity of the drug, or prospective genotyping and prospective phenotyping.

Claim 167 (withdrawn). The method of claim 143, wherein: the moiety Y is a first drug; and redesigning the first drug results in a second drug with fewer side-effects or an increased therapeutic index as compared to the first drug.

Claim 168 (withdrawn). The method of claim 1, wherein the drug is selected from among troglitazone, rosiglitazone, pioglitazone, methotrexate, atorvastatin, celecoxib, refecoxib and cerivastatin.

Claim 169 (previously presented). The method of claim 1, wherein said exposure comprises activation with light.

Claim 170 (cancelled).

Claim 171 (withdrawn). The method of claim 22, where B is a single stranded DNA or RNA and the number of sequence permutations is equal to  $4^i$ , wherein i is about 2 to about 25.

Claim 172 (withdrawn). The method of claim 171, where i is about 3 to about 5, 6, 7 or 8.

Claims 173 - 174 (cancelled).

Claim 175 (cancelled).

Claim 176 (New). The method of claim 1 wherein X is an aryl azide and Z is serine, threonine, lysine, tyrosine, glutamic acid, aspartic acid or cysteine; and Q comprises biotin or an oligonucleotide.

Claim 177 (New). The method of claim 1, wherein X is one of

